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Equivalents: ;

ABSTRACT:

A wound dressing comprises a free-flowing, anhydrous particulate material, which on contact with water forms a water-soluble hydrogel. The particulate material is preferably a cellulose derivative and may include a wound healing therapeutic agent such as growth factors or antibiotics. At least 50% of the particles by weight will pash through a mesh of size 18 (1mm). In use the particulate material is sprinkled onto a wound where it absorbs the exudate and forms a gel which can be removed by washing.

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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

WO 03/061538 A1

(54) Title: PARTICULATE WOUND DRESSINGS

(57) Abstract: A wound dressing consisting essentially of a free-flowing, substantially anhydrous particulate material, wherein the particulate material forms a water-soluble hydrogel in contact with water. In use, the dressing is sprinkled onto an exuding wound where it absorbs wound fluid to form a continuous hydrogel layer over the wound.

# PARTICULATE WOUND DRESSINGS

The present invention relates to particulate wound dressing materials for application to wound by sprinkling onto the wound surface.

It is known that the maintenance of a moist wound environment promotes the healing of wounds, especially burns and chronic wounds such as ulcers. However, it is also desirable to avoid excessive moisture or pooling of wound exudate on the wound, since liquid exudate causes maceration of skin adjacent to the wound and other difficulties. Furthermore, the liquid exudate can leak from the wound site and contaminate clothes or bedding.

In practice, it is difficult to maintain the desired moisture level at the wound site because the rate of wound fluid production varies from wound to wound and over time for any single wound. This can necessitate frequent dressing changes and a range of dressing types to treat different wounds. Dressing changes are undesirable for a number of reasons, including cost, potential for infection, and additional wound trauma where the dressing is adhered to the wound.

A wide variety of dressing materials have been used for wound covering, many of which are currently commercially available. One such class of wound dressings is the absorptive hydrogel dressings. These consist of sheets of hydrophilic polymers such as gelatin, alginates or polyacrylamides, which can absorb several times their own weight of wound fluid to form a stable water-insoluble gel. Hydrogel dressings of which type include INTRASITE (Registered Trade Mark of Smith & Nephew, UK) and VIGILON (Registered Trade Mark of C.R. Bard, USA.). The hydrogel sheets are not always sufficiently flexible to conform to all wound surfaces. The absorptive capacity of the hydrogel sheets is predetermined and limited, and removal of the hydrogel after use can be difficult.

Also known are the so-called hydrocolloid dressings. These comprise gel-forming hydrocolloid particles of gelatin, pectin or the like embedded in an

adhesive matrix. These dressings have high absorptive capacity, but may nevertheless induce undesirable side reactions due to the matrix material.

WO00/12144 describes particulate compositions capable of forming coherent, insoluble hydrogels in contact with wound fluid. The compositions are mixtures of two water soluble polymers that react in the presence of water to form an insoluble gel, for example a mixture of sodium carboxymethyl cellulose and chitosan. A further particulate composition of this type is COMFEEL (Registered Trade Mark) powder, supplied by Coloplast AS, which is a mixture of sodium carboxymethyl cellulose, guar gum and xanthan gum. In use, the powder is spread over the wound bed where it reacts with water to form an absorbent, insoluble gel. When a dressing change is desired, the insoluble gel on the wound bed is physically removed along with the secondary dressing covering the wound.

It is an object of the present invention to provide dressings for use in the treatment of a wide range of wounds.

The present invention provides a wound dressing consisting essentially of a free-flowing, substantially anhydrous particulate material, wherein the particulate material forms a water-soluble hydrogel in contact with water.

The free-flowing particulate material can be poured or sprinkled over a wound, where it absorbs wound exudate to form a soft, continuous, conformable layer of water-soluble hydrogel over the wound. The gel is both absorbent and protective, and also functions as a fluid reservoir to preserve a moist wound surface. The gel eases the debridement of dead tissue and promotes epithelialisation. The gel is particularly easy to remove at dressing changes by simply irrigating with water or saline.

The particulate material consists essentially of the water-soluble hydrogel-forming material. Suitable materials are materials that form a viscous liquid or a gel with water under physiological conditions of temperature and pH. Such hydrogel forming materials are normally medically acceptable macromolecular materials

that have the ability to swell and absorb fluid to form a gel structure that is soluble at higher water concentrations. The hydrogel may be a biopolymer, and/or it may be bioabsorbable. That is to say, it may undergo gradual resorption *in vivo*. At higher concentrations, the material preferably forms a gel with water. This gel state can be distinguished from the solution state by its physical characteristics (it bounces rather than flows) and by its thermal properties, since it should exhibit a distinct melting point above 25ºC in differential scanning calorimetry. Suitable materials can absorb up to 10 times, or even 15 times or 25 times their weight of saline to form the said gel.

The particulate materials are normally substantially free from water-insoluble components, or mixtures of components that react in solution to form insoluble gels, or support materials such as gauzes, films or foams that normally make up wound dressings. Preferably at least 90% by weight, more preferably at least 95% by weight, and most preferably at least 99% by weight of the particulate material consists of one or more water-soluble macromolecular materials.

Preferably, the particulate material is selected from the group consisting of sodium carboxymethyl cellulose, carboxymethyl cellulose, ethyl cellulose, hydroxyethyl cellulose, methylhydroxyethyl cellulose, hydroxypropyl cellulose, hydroxyproplyethyl cellulose, cetyl hydroxyl cellulose, carboxymethyl hydroxethyl cellulose, methyl cellulose, carrageenan, pectin, nitrocellulose, soluble polyacrylates, guar gum derivatives, sodium alginate, and mixtures thereof.

The particles (and thereby the wound dressing) are substantially anhydrous. That is to say, the particles preferably comprise less than 20% by weight of water, more preferably less than 10% by weight of water. The anhydrous particles have greater absorptive capacity for wound fluid, and are more free-flowing than hydrated particles. Furthermore, the anhydrous particles are more stable towards sterilization by gamma-irradiation.

The particles are small enough to form a uniform coating when sprinkled over a wound. The free flowing nature of the particles enables them to coat a wide

variety of wound surfaces and shapes. Preferably a weight fraction of at least about 50% of the particles, more preferably at least about 90% of the particles and most preferably substantially all of the particles have mesh sizes in the range about 70 to about 1000 micrometers, preferably about 300 to about 700 micrometers. Preferably, a weight fraction of at least about 50% of the particles, more preferably at least about 90% of the particles and most preferably substantially all of the particles has a ratio of the largest dimension to the smallest dimension (aspect ratio) of less than about 10, more preferably less than about 5, and most preferably of less than about 3, in order to optimise the free-flowing nature of the dressing.

In certain embodiments the wound dressing according to the present invention is medicated. That is the particles comprise a wound healing therapeutic agent dispersed therewith or therein. Typically, the wound healing therapeutic agent is selected from the group consisting of antimicrobial agents, growth factors, analgesics, steroids and mixtures thereof. Preferably, the wound healing therapeutic agent comprises an antimicrobial selected from the group consisting of antibiotics, chlorhexidine, silver sulphadiazine, triclosan and povidone iodine. Preferably, the wound healing therapeutic agent or agents are present in an amount of from 0.01% to 10% by weight of the dressing, more preferably from 0.1% to 2% by weight of the dressing.

Preferably, the particulate wound dressing according to the present invention is not a freeze-dried gel. That is to say, preferably the particulate wound dressing has not been made by freeze drying (lyophilizing) an aqueous solution or gel of the components.

As already noted, the dressing according to the present invention is easy to sterilize due to its anhydrous nature, and this also makes it storage-stable. Accordingly, the wound dressing is typically sterile and packaged in a microorganism-impermeable container. The package may comprise a dispenser region having a plurality of holes for sprinkling the particles of the dressing directly from the package.

Preferably, the package is a single-use package, for example a package containing less than 25g of the particulate material, preferably from 1 to 15g of the particulate material and more preferably from 2 to 10g of the particulate material.

The present invention further provides the of a free-flowing, water-soluble, substantially anhydrous particulate material that forms a water-soluble hydrogel in contact with water for the preparation of a wound dressing for application to a wound by sprinkling of said particulate material onto the wound bed.

Preferably, the step of sprinkling is followed by covering the sprinkled particulate dressing with an absorbent secondary dressing. This helps to retain the sprinkle dressing in place, and prevents leakage in the case of highly exuding wounds that cause the hydrogel to dissolve completely.

Suitable wounds for treatment in this way include burns or chronic wounds such as pressure sores, venous ulcers or diabetic ulcers.

Preferably, the wound dressing according to this aspect of the invention is a wound dressing in accordance with one or more of the preferred features of the wound dressing according to the present invention.

In a further aspect, the present invention provides a method of treatment of a wound in a mammal, comprising applying to the wound a layer of a wound dressing according to the present invention.

An embodiment of the present invention will now be described further, by way of example.

Example 1

A wound dressing according to the invention consists of particles of substantially anhydrous sodium carboxymethyl cellulose available from Hercules Inc. under the Registered Trade Mark AQUASORB. 5g of this material of sieve size about 300 to

about 700 micrometers is mixed with 2%w/w of silver sulfadiazine powder, packaged in a microorganism-impermeable foil pouch and sterilized by gamma irradiation.

In use, the material is sprinkled onto the exuding wound at a generally uniform thickness, typically about 0.5 to 5 mm thick, preferably 1 to 3 mm dry thickness, corresponding to a density of 0.02 to 0.2 are preferably 0.05 to 0.1g/cm$^2$. The material absorbs the exudate to form a sticky gel layer that is flexible and breathable, and that swells and absorbs further exudate. The hydrogel layer completely covers the wound, but can be removed easily by washing with water or saline. A further advantage of this dressing is that, if exudate production exudes the capacity of the hydrogel, then instead of pooling under the hydrogel, the hydrogel layer simply dissolves and can be taken up in an absorbent secondary dressing over the hydrogel layer.

The above example is for the purpose of illustration only. Many other embodiments falling within the scope of the accompanying claims will be apparent to the skilled reader.

CLAIMS

1. A wound dressing consisting essentially of a free-flowing, substantially anhydrous particulate material, wherein the particulate material forms a water-soluble hydrogel in contact with water.

2. A wound dressing according to claim 1, wherein the particulate material is selected from the group consisting of sodium carboxymethyl cellulose, carboxymethyl cellulose, ethyl cellulose, hydroxyethyl cellulose, methylhydroxyethyl cellulose, hydroxypropyl cellulose, hydroxyproplyethyl cellulose, cetyl hydroxyl cellulose, carboxymethyl hydroxethyl cellulose, methyl cellulose, carrageenan, pectin, nitrocellulose, and guar gum derivatives.

3. A wound dressing according to any preceding claim, wherein at least 50% of the particles by weight will pass a mesh of size 18 (1 mm).

4. A wound dressing according to any preceding claim, wherein the particles comprise a wound healing therapeutic agent.

5. A wound dressing according to claim 4, wherein the wound healing therapeutic agent is selected from the group consisting of antimicrobial agents, growth factors, analgesics, steroids and mixtures thereof.

6. A wound dressing according to claim 4, wherein the wound healing therapeutic agent comprises an antimicrobial selected from the group consisting of antibiotics, chlorhexidine, silver sulphadiazine and povidone iodine.

7. A wound dressing according to any preceding claim, which is sterile and packaged in a microorganism-impermeable container.

8. Use of a free-flowing, water-soluble, substantially anhydrous particulate material that forms a water-soluble hydrogel in contact with water for the

preparation of a wound dressing for application to a wound by sprinkling of said particulate material onto the wound bed.

9. Use according to claim 8, wherein said sprinkling is in an amount of from about 0.02 to about 0.2 g/cm$^2$.

10. Use according to claim 9, wherein said step of sprinkling is followed by covering the sprinkled particulate dressing with a secondary dressing.

11. Use according to claim 9 or 10, wherein said wound is a burn or a chronic wound.

# INTERNATIONAL SEARCH REPORT

Int nal Application No
PCT/GB 03/00197

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61F13/00 A61F13/02 A61L15/03

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61F A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| A | US 5 902 600 A (JONES DAVID P ET AL) 11 May 1999 (1999-05-11) * abstract * | 1-7 |
| A | US 4 393 048 A (MASON JR ARTHUR D ET AL) 12 July 1983 (1983-07-12) * abstract * column 1, line 12 - line 13; claim 1 | 1-7 |
| A | US 4 391 799 A (MASON JR ARTHUR D ET AL) 5 July 1983 (1983-07-05) * abstract * column 1, line 11 - line 12 | 1-7 |
| A | WO 00 12144 A (NIELSEN BRIAN ;COLOPLAST AS (DK)) 9 March 2000 (2000-03-09) page 3, line 5 - line 25 | 1-7 |

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 7 April 2003 | 17/04/2003 |

| Name and mailing address of the ISA | Authorized officer |
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| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: (+31-70) 340-3016 | Settele, U |

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 03/00197

## Box I Observations where certain claims w re found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 8-11
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Int. ... Application No
PCT/GB 03/00197

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---|---|---|
| US 5902600 A | 11-05-1999 | NONE | |
| US 4393048 A | 12-07-1983 | NONE | |
| US 4391799 A | 05-07-1983 | NONE | |
| WO 0012144 A | 09-03-2000 | AU 5279299 A | 21-03-2000 |
| | | WO 0012144 A1 | 09-03-2000 |
| | | EP 1109584 A1 | 27-06-2001 |